

Applicant : Tamar H. Michaeli  
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Page 6

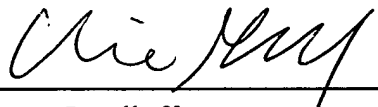
Conclusion

Applicant requests examination of the claims as amended. Should there be any minor matters preventing such examination, applicant requests that the Examiner contact the attorney indicated below.

Respectfully submitted,

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Appendix  
Marked up amendments  
Continuation of U.S. Patent Application 09/245,169, Filed February 27, 2002  
Added material is underlined; deleted material is bracketed.

In the Specification:

On page 14, the paragraph on lines 7-11 has been amended as follows:

Figure 5. Figure 5 depicts the DNA sequence of a PDE1C cDNA (SEQ ID NO:1) that confirms that PDE1C is expressed in pancreatic islet  $\beta$ -cells. Reverse transcriptase polymerase chain reaction was used to amplify and clone a fragment of the PDE1C mRNA common to all known PDE1C isozymes.

On page 28, the two paragraphs on lines 10-25 have been amended as follows:

--Reverse transcriptase polymerase chain reaction (RT-PCR) analysis. RT-PCR analysis was performed on 5  $\mu$ g of RNA prepared from  $\beta$ TC3 cells using Trizol (Gibco-BRL). Controls lacking reverse transcriptase were included in the reactions. To determine expression of PDE1C the following oligonucleotides were used: for RT - oligo dT; and for PCR amplification - JWPDE1C-5 5'-ACAGGGCAGAGGAGATCAAGTTT (SEQ ID NO:2); and JWPDE1C-3 5'-CTTTTCGCCTGCCTTTTCTCCTT (SEQ ID NO:3). The 408 bp PCR product was cloned and its DNA sequence was determined.

The following oligonucleotides were used for PCR amplification to determine the expression of PDE4A: JWPDE4A-5 5'-AGCCATGGAACAGTCAAAGGTCAA (SEQ ID NO:4); and JWPDE4A-3 5'-TCAGGAGGGCCAGGAGTCGT (SEQ ID NO:5); and to determine the expression of PDE4D: JWPDE4D-5 5'-GAGGGCCGGCAGGGACAGAC (SEQ ID NO:6); and JWPDE4D-3 5'-GGGGGTGGGGTGGGTGAGAGG (SEQ ID NO:7). Amplification products 436 AND 470 bp long were obtained for PDE4A and D, respectively.--